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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/383,114	08/25/1999	JOHN A. ARCADI	35687/RW/H29	6120

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CHRISTIE, PARKER & HALE, LLP
350 WEST COLORADO BOULEVARD
SUITE 500
PASADENA, CA 91105

EXAMINER	
COOK, REBECCA	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/383,114	ARCADI, JOHN A.	
	Examiner	Art Unit	
	Rebecca Cook	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

Claims 1, 20-24, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using Rhodamine-123 to treat prostate cancer, does not reasonably provide enablement for any and all carcinomas. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to chemotherapy, and the relative skill of those in the art is high, generally that of a PHD or MD. This unpredictability has a number of facets, as discussed hereinafter.

Treatment by Cancer Type

While the state of the art is relatively high with regard to the treatment of specific cancers with specific agents, it has long been underdeveloped with regard to the treatment of cancers broadly. In particular, there is no known anticancer agent which is effective against all cancers. This is why the National Cancer Institute (NCI) has the extensive *in vitro* drug screening program it does. As discussed by the court in In re Brana, 51 F.3d 1560 (Fed. Cir. 1995), *in vitro* assays are used by NCI (such as the P388 and L1210 lymphocytic leukemia tests at issue therein) to measure the potential antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) *Id.* at 1567-68. These *in vitro* tests are considered reasonably correlative of success *in vivo*.

Thus, a considerable amount of *in vitro* empirical testing is required, with no *a priori* expectation of success being present, before a candidate anticancer agent can be considered useful against any particular cancer type.

2. The breadth of the claims

The claims are very broad and inclusive of all carcinomas.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides direction only for the treatment of prostate cancer.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to the actual treatment of all cancers in a mammal with the claimed compounds fails to rebut the presumption of unpredictability extant in this art. Applicants fail to provide the guidance and information required to ascertain which particular type of cancer the claimed anticancer agent will be effective against without resorting to undue experimentation. Applicant's limited disclosure of the treatment of carcinomas (see the fifth line from the bottom of page 20) is noted but is not sufficient to justify claiming all cancers broadly.

Absent a reasonable *a priori* expectation of success for using a specific chemotherapeutic agent/combination to treat any particular type of cancer, one skilled in the art would have to extensively test many various tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Claims 9-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1) Nature of the invention.

The claims are drawn to a solution comprising ethyl alcohol and Rhodamine-123 dissolved in water.

2) State of the prior art.

The references do not indicate that solutions of ethyl alcohol and Rhodamine-123 are known in the art

3) Level of ordinary skill in the art.

The level of ordinary skill in the pharmaceutical art is high, generally that of a PHD or MD.

4) Level of predictability in the art.

The art pertaining to the preparation of pharmaceutical solutions remains highly unpredictable. Processes of preparing different types pharmaceutical solutions require different types of testing. There is little predictability as to which solvents will yield a favorable outcome. In the instant solution comprising ethyl alcohol and Rhodamine-123 EMBASE 94120900 discloses that ethanol causes intravenous toxicity.

5) Amount of direction and guidance, working examples and quantity of experimentation needed.

Page 12 discloses a stock solution comprising 95% ethyl alcohol and 5 (?) water and a treatment solution of 1% ethyl alcohol. Page 14 discloses a solution comprising 5% alcohol and 5% glucose. It is not clear that ethanol is the alcohol.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not perform the claimed process without undue experimentation, see In re Armbruster 185 USPQ 152 CCPA 1975.

Claims 3-8, 10-13, 15-16, 18-24, 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 3, 4, 10, 20, 26 and 27, the word "including" renders the claims indefinite because it is unclear whether the limitations(s) following the word are part of the claimed invention.

The word "A" in claims 3-8, 10-13, 15-16, 18-19, 21-24, 26 and 28 renders the claims confusing as to whether they are dependent or independent claims. Amending them to recite "The" will overcome this rejection.

Claim Rejections - 35 USC § 103

The earlier rejections under 35 USC 103(a) are withdrawn in favor of the following rejection. In view of this, applicant's arguments are moot.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernal or Arcadi (J. Surg. Onc. 1990) in view of 5,880,141 (Tang et al) ~~and~~ or EMBASE 94148842 and further in view of MEDLINE AN 93172422.

Bernal (abstract, Table I, Figure I) discloses that Rhodamine-123 exhibits anticarcinoma activity. Arcadi (abstract, Table I, Materials and Methods, Conclusion) discloses that Rhodamine-123 in saline solution is effective against prostate cancer.

The instant claims differ over the reference in reciting a solvent which has ethyl alcohol and measuring the PSA level. Dependent claims recite dosage amounts, treatment regimens and the use of sugar in the solution.

However, Tang (column 11, line 60 through column 12, line 2) discloses that a cosolvent system comprising ethanol and dextrose (D5W) in water is known in the pharmaceutical art. Furthermore, EMBASE 94148842 (abstract, lines 7-8) disclose that ethanol enhances drug solubility. Therefore, in the absence of a showing of unexpected results commensurate in scope with the claims it would be obvious to one of ordinary skill in the art to use the Rhodamine-123 of Bernal or Arcadi in a solution comprising the ethanol and dextrose in water of Tang or ethanol of EMBASE 94148842 to yield the instant solution and its method of use.

Furthermore, once a method of use of a compound is known it is within the skill of the artisan to determine the optimum dosage amounts and treatment regimens. Additionally, MEDLINE AN 93172422 discloses that it is well-known to measure PSA both pre and post treatment in the management of prostate cancer.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cook whose telephone number is (571) 272-0571. The examiner can normally be reached on Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (571) 272-0584.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Renee Pettus (571) 272-0547 in Customer Service.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rebecca Cook

Primary Examiner
Art Unit 1614